WO 03/089136 PCT/EP03/50114

## CLAIMS

- 1. Substrate plate, comprising a microplate (1) made of a plastic material, having an array of wells (2) arranged in rows and columns, the bottom of at least one well (2) being provided by a porous substrate (3), characterised in that each porous substrate (3) is incorporated into the well (2) by means of a thermal bond.
- 2. Substrate plate according to claim 1, wherein the porous substrates (3) comprise oriented flow-through channels.
- 3. Substrate plate according to claim 1 or 2, wherein each well (2) is formed in a discrete protrusion, projecting from one face (7) of the microplate (1), a separate porous substrate (3) being bonded to the distal end of each protrusion facing away from the face (7), in such a manner that the porous substrates (3) are spaced apart from each other.
  - 4. Substrate plate according to any one of the preceding claims, wherein the porous substrates (3) are made of a metal oxide material.
- 5. Substrate plate according to claim 4, wherein the porous substrates (3) are made of aluminium oxide.
  - 6. Substrate plate according to any one of the preceding claims, wherein the plastic material comprises a cyclic olefin copolymer, in particular a grade of TOPAS®.
- 7. Method of manufacturing a substrate plate according to any one of the preceding claims, comprising heating the porous substrates (3) and bringing the microplate (1) and porous substrates (3) into contact with each other.
- 8. Method according to claim 7, comprising supplying heat to the porous substrates (3) whilst the microplate (1) is in contact with the porous substrates (3).

- 9. Method according to claim 7 or 8, comprising pressing the microplate (1) and the porous substrates (3) against each other.
- 10. Method according to claim 9, comprising cooling the porous substrates (3) whilst pressing the microplate (1) and the porous substrates (3) against each other.
- 11. Method according to any one of claims 8-10, comprising cooling the porous substrates (3) by decreasing the rate at which heat is supplied to the porous substrates (3) in a controlled manner.

10

25

30

35

- 12. Method according to any one of claims 7-11, comprising arranging a plurality of porous substrates (3) in an array of rows and columns, corresponding
- substantially to at least part of the array of rows and columns in which the wells (2) in the microplate (1) are arranged, bringing the microplate (1) and array of porous substrates (3) into alignment in such a manner that each porous substrate (3) is aligned opposite the bottom of a well (2), and bringing the microplate (1) into contact with the porous substrates (3) in such a manner that each porous

substrate (3) closes off the bottom of one well (2).

- 13. Method according to claim 12, comprising cutting the substrates (3) from a sheet of porous substrate material.
- 14. Method according to claim 13, wherein the step of cutting the substrates (3) from the sheet of porous substrate material comprises placing the sheet of substrate material in a holder, comprising a plurality of collection sites for receiving substrates (3) cut from the sheet of porous substrate material, the collection sites being arranged in an array of rows and columns corresponding substantially to at least part of the array of rows and column in which the wells (2) in the microplate (1) are arranged, wherein the step of arranging the plurality of porous substrates (3) comprises receiving the porous

WO 03/089136 PCT/EP03/50114 23

substrates (3) cut from the sheet of porous substrate material in the collection sites.

- 15. Method according to any one of claims 7-11, comprising providing a sheet (23) of porous substrate material comprising the substrates (3), bonding the sheet (23) to the microplate (1), and removing all porous substrate material interconnecting the porous substrates (3).
- 16. Method according to any one of claims 7-14, 10 comprising bonding a microplate (1) in which each well (2) is formed in one of an array of spaced protrusions, arranged in rows and columns and projecting from one face (7) of the microplate (1), wherein each porous substrate (3) is bonded to the distal end of each 15 protrusion facing away from the face (7), the method comprising mounting the microplate (1) in a guide (27;30), adapted to envelope at least parts of side walls (13) connecting the face (7) to the distal end of a corresponding one of the protrusions, such that at least 20 part (13) of a protrusion is supported by the guide (27;30).
  - 17. Method according to any one of claims 7-16, comprising pressing the microplate (1) against the porous substrates (3) by applying a support (24) against the microplate (1), comprising an array of support protrusions (25;34) arranged in rows and columns and corresponding substantially to the array of wells (2), each support protrusion (25;34) being shaped to engagingly fit inside the well (2), such that walls (26) of each well (2) are supported from inside the well (2) by the support protrusions (25;34), when inserted into the wells (2).

25

30

35

18. System for conducting bioassays, comprising a substrate plate with a number of wells (2), and an incubation device (8) for holding the plate, characterised in that the substrate plate comprises a microplate (1) with an array of wells (2) arranged in rows and columns, wherein the bottom of each well (2) is a porous microarray

WO 03/089136 PCT/EP03/50114

substrate (3), wherein the incubation device (8) comprises an incubation chamber (9) for holding the microplate (1) and a cover (10) for sealing the incubation chamber (9), said incubation device (8) having a heat block (11) with an array of openings (12), each opening (12) adapted to receive a well (2) of the microplate (1), wherein a sealing gasket (20) is provided for individually sealing each well (2) of the microplate (1), and in that the system comprises a substrate plate according to any one of claims 1-6, or a substrate plate manufactured by means of a method according to any one of claims 7-17.

19. Apparatus for manufacturing a substrate plate according to any one of claims 1-6, comprising a heating device (38,40) for heating the porous substrates (3) and a press for pressing the microplate (1) and the porous substrates (3) against each other.

15

35

- 20. Apparatus according to claim 19, wherein the press comprises a heated plate (38), the heated plate (38) comprising a plurality of protruding rims (39), each arranged in a shape corresponding to a perimeter of a porous substrate (3) and substantially centred on a well (2) of the microplate (1), the rims (39) being arranged to contact a part of a face of a porous substrate (3) facing away from the microplate (1) near the perimeter of the porous substrate (3).
  - 21. Apparatus according to claim 19, suitable for manufacturing a substrate plate in which the porous substrates (3) lie substantially in a plane, wherein the heating device comprises a heating surface (22;38), arranged to contact a face (5) of the porous substrates (3) facing away from the microplate (1).
  - 22. Apparatus according to any one of claims 19-21, further comprising a controller for decreasing the rate at which heat is supplied to the porous substrates (3) in a controlled manner.
  - 23. Apparatus according to any one of claims 19-22, wherein the press comprises a support (24) to

WO 03/089136 PCT/EP03/50114

be applied against the microplate (1) and a guidance mechanism (27,28) for aligning the support (24) relative to the porous substrates (3) in a plane perpendicular to the direction of pressing.

- 24. Apparatus according to claim 23, wherein the guidance mechanism comprises spacing means (28) for limiting the movement of the support (24) in the direction of pressing to a pre-determined distance from the substrates (3).
- 25. Apparatus according to any one of claims 19-24, wherein the press comprises a support (24) to be applied against the microplate (1) and the support (24) comprises an array of support protrusions (25;34) arranged in rows and columns and corresponding substantially to the array of wells (2), each support protrusion (24;34) being shaped to engagingly fit inside the well (2), such that walls (26) of each well (2) are supported from inside by the support protrusions (25;34), when inserted into the wells (2).
- 26. Apparatus according to any one of claims 19-25, suitable for bonding a microplate (1) in which each well (2) is formed in one of an array of spaced protrusions, arranged in rows and columns and projecting from one face (7) of the microplate (1), and arranged to bond each porous substrate (3) to the distal end of each protrusion facing away from the face (7), which apparatus comprises a guide (27;30) for mounting the microplate (1), adapted to envelope at least parts of side walls (13) connecting the face (7) to the distal end of a corresponding one of the protrusions, such that at least part of a protrusion is supported by the guide (27;30).
  - 27. Apparatus according to claim 26, wherein each guide comprises one or more overhangs (32), arranged to cover a part (41) of a surface on the distal end of at least one protrusion to which a porous substrate (3) is to be bonded, the covered part (41) being complementary in shape to a porous substrate (3).